Effect of Preoperative Dexamethasone before Total Thyroidectomy on Postoperative Nausea, Vomiting, Pain and Voice Dysfunction

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ABSTRACT

Background: *Thyroidectomy is one of the most common surgical procedures in the world. After thyroidectomy postoperative nausea and vomiting (PONV), and so pain is high. Voice dysfunction can also occur.* ***Aim:*** *The aim of this study is to assess the effects of a preoperative single dose of Dexamethasone on postoperative nausea, vomiting, pain and vocal dysfunction in patients undergoing total thyroidectomy.* ***Patients and methods:*** *A prospective randomized comparative study was done from September 2014 to February 2016 in Ain shams university hospital (a tertiary care hospital) , general surgery department (endocrine surgery unit), Cairo, Egypt. The study included one hundred patients suffering from thyroid diseases for which total thyroidectomy was indicated. Patients were divided into two groups: Group A: received preoperative prophylactic dexamethasone. Group B: didn't receive preoperative prophylactic dose of dexamethasone. Preoperative workup included History taking, Examination; general and local, preoperative investigations including laboratory and radiological. ECG, Echocardiography and pulmonary function tests when indicated. Vocal cord and voice function evaluation (1. direct laryngoscopy, 2. Voice Recording, 3. Aerodynamics (F0, Jitter and Shimmer). Patients were put into 2 treatment groups; group1 received 8 mg/2 mL of Dexamethasone and the control group 2 received 2 mL NaCl 0.9% each in 100 mL of physiologic saline given intravenously (I.V.). Post-Operatively, patients were assessed for nausea, vomiting, pain and voice changes done together with search for any postoperative complications. This was done postoperatively and at regular visits conducted at 2 weeks, 1, 2, 4 and 6 months.* ***Results:*** *The study included 100 patients. Group (A) included 47 patients and group (B) included 53 patients. There was no statistically significant difference between both groups as regards age, sex, Baseline voice recording (preoperative voice recordings), while post-operative voice recording showed significant changes in results of dysphonia with P value 0.025 in dexamethasone group (post-operative improvement), although other voice recording parameters showed no significant changes compared to preoperative levels. Pre-operative (base line) aerodynamics showed no significant difference between the two groups and so postoperative analysis of aerodynamics which showed close results as regard fundamental frequency and Jitter except for the Shimmer values which showed statistically significantly different values between the two groups. Post-operative dyspepsia study showed that 12.5 % of patients who didn't receive dexamethasone experienced various degrees of dyspepsia while no patients from the other group suffered from dyspepsia, however the results were not statistically significant. Postoperative pain showed a highly significant difference between the dexamethasone group and the other group where Group (A) patients showed lower values of average pain.* ***Conclusion:*** *A preoperative single dose of dexamethasone can significantly reduce nausea, vomiting, and pain, and improve postoperative voice function so that this strategy can be routinely applied in thyroidectomy operations.*

Key words: *thyroidectomy, nausea, vomiting and voice dysfunction.*

INTRODUCTION

Thyroidectomy is considered one of the most common elective surgical procedures in the western world. Estimates of 50,000 thyroidectomies are performed yearly in the United States[(1)]. Unlike other surgical interventions, where the incidence of postoperative nausea and vomiting is below 30%[(2)], after thyroidectomy incidence of postoperative nausea and vomiting (PONV) reaches up to 70- 80% when no prophylactic antiemetic therapy is given[(3)]. PONV is not only uncomfortable for patients but also repeated

vomiting can lead to postoperative bleeding with subsequent airway obstruction and potential re-operation [(4)]. Dexamethasone which is an adrenocortical steroid is regularly used against chemotherapy-induced nausea [(5)] and has shown effectiveness against postoperative nausea in several studies [(6)].

Another important and feared complication of thyroid surgery is vocal dysfunction. Operative injury to the recurrent laryngeal nerve was often considered to be the main cause of voice alterations and its prevalence varies from 0.77% to 13.3%. However, change in vocal quality can also be found in the absence of laryngeal nerve injury [(7)].

The aim of our study is to assess the effect of a preoperative single dose of Dexamethasone on postoperative nausea, vomiting, pain and vocal dysfunction in patients undergoing total thyroidectomy.

PATIENTS AND METHODS

A prospective randomized comparative study was done from September 2014 to February 2016 in Ain shams university hospital (a tertiary care hospital), general surgery department (endocrine surgery unit). Cairo, Egypt. The study included one hundred patients suffering from thyroid diseases for which total thyroidectomy was indicated. Inclusion criteria included; Thyroid disease to which total thyroidectomy is indicated (e.g. Multinodular goiter with cosmetic or pressure symptoms), Age more than 18 years, No known malignant thyroid disease, Normal preoperative voice analysis (normal voice recording and aerodynamics) , No previous neck or thyroid surgery, and all the patients should had signed the informed consent. Exclusion Criteria included; Patients with chronic pain disorder. Insulin dependent diabetes mellitus, History of chronic nausea or vomiting due to other medical conditions, Pregnancy, Patients with previous voice disturbance or voice visual analog scale > 40, Patients with proved post-operative recurrent laryngeal nerve injury, and those not fulfilling the inclusion criteria.

Patients were randomly divided using closed envelopment method into two groups:

- **Group A:** (47 patients) received preoperative prophylactic Dexamethasone.
- **Group B:** (53 patients) didn't receive preoperative prophylactic dose of Dexamethasone.

Preoperative workup included History taking (smoking, history of previous operations, other system review, Presenting indication for total thyroidectomy), Examination; general and local, preoperative investigations including laboratory and radiological. ECG, Echocardiography and pulmonary function tests when indicated. Vocal cord and voice function evaluation by;

i. Direct laryngoscopy, rigid laryngoscopic examination 90 degree or nasofibroscopy can be used if failed direct laryngoscopy. **ii. Voice Recording:** Intonation was recorded preoperatively and at the same postoperative time points as nausea and pain. **iii. Aerodynamics (F0, Jitter and Shimmer):** the overall objective vocal quality of the subjects was measured by means of Dysphonia Severity Index (DSI) which is designed to establish an objective and quantitative correlate of perceived vocal quality. It is based on the combination of the following set of voice measurements; fundamental frequency (F0 Hz), mean percent Jitter and shimmer. (**Jitter measurements:** It is measure of the cycle-to-cycle variations of fundamental frequency) (Shimmer measurements: It is measure of the cycle-to-cycle variations of amplitude).

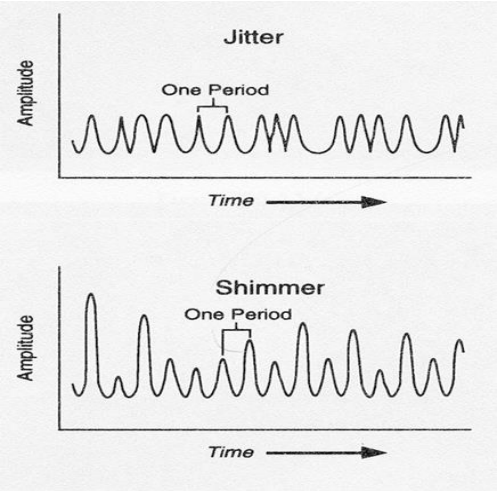

Fig. (1): Jitter and Shimmer measurement.

Patients were put into 2 treatment groups; group1 received 8 mg/2 mL of Dexamethasone and the control group 2 received 2 mL NaCl 0.9% each in 100 mL of physiologic saline given intravenously (I.V.). Dexamethasone 8 mg is the minimum effective dose for the reduction of postoperative nausea and vomiting. The treatment and control solutions were prepared off the ward, appeared transparent, and were marked identically. The infusions were given over 15 minutes by a blinded nursing staff, 45 minutes before the initiation of anesthesia. Thus, the patient, the nurse and the anesthesiologist were all blinded.

Operative workup:

All patients received standard general anesthesia with endotracheal intubation. The operations were all done by a senior staff. After anesthesia patients were put in supine position with hyperextended neck, Skin preparation and draping. Transverse collar incision of skin, opening of subcutaneous tissue including platysma muscle, opening of investing layer of deep cervical fascia, dissection of the gland with ligation of middle thyroid vein then ligation of superior and inferior thyroid vessels followed by separation of the gland from recurrent laryngeal nerve, trachea with surrounding structures, hemostasis and closure in layers with drain.

Post-Operative work up:

The patients were followed up after the operation. Proper observation and clinical assessment as regards the general vital data (pulse, blood pressure, temperature and respiratory rate), condition of the wound and attention directed for detection of any complications. The patients were discharged after resuming full oral diet, drains removed and assuring that no early post-operative complications exist. Postoperative visits were conducted at 2weeks, 1, 2, 4 and 6 months. In each visit assessment of nausea, vomiting, pain and voice changes was done together with search for any postoperative complications.

Nausea and vomiting were assessed on a 4 point scale (0- no nausea, 1- mild nausea, 2- severe nausea, 3- vomiting). Antiemetic therapy was given according to the patient needs. The first-line antiemetic was 20 mg Metoclopramide i.v.; the second line was 4 mg Ondansetron i.v.. The use of postoperative antiemetic (frequency, amount of intake, and substance) were recorded during the entire observation period. Pain was assessed with a standardized Visual Analogue scale (VAS) that ranged from 0 (no pain) to 10 (worst pain imaginable) at the above-mentioned time points. After surgery, all patients received basic analgesic therapy only on demand with acetaminophen up to 2 g/d. additionally, some patients received Nalufen or Pethidine (second line), given i.v. or intramuscular. The administration of postoperative analgesics (frequency, amount of intake, and substance) was recorded. Voice function was evaluated by Direct laryngoscopy 2 days after the operation, rigid laryngoscopic examination 90 degree or nasofibroscopy were used if failed direct laryngoscopy, Voice recording, Aerodynamics (F0, Jitter and Shimmer), Auditory perception assessment (APA), subjective impression of voice (0-best, 1-Mild, 2- Moderate, 3- Severe, 4- worst) were done to the patients. Patients with proved postoperative laryngeal nerve injury were excluded from the study. Patients with proved postoperative voice changes were reevaluated by the same procedures at postoperative visits 2 weeks, 1, 2, 4, 6 months.

All the data were recorded, tabulated and statistically analyzed emphasizing on; Preoperative data including patient age and sex, surgical indication for thyroidectomy , pre-operative neck ultrasound, preoperative biopsy if taken and results of preoperative voice assessment, Operative data including operative time as measured from first skin incision to the application of dressings, anesthetic or surgical complications if present, Post-operative data including post-operative pain, the need for analgesia, nausea, vomiting and need for anti-emetics, voice functions, length of hospital stay and post-operative complications.

Statistical Methods:

- Data were analyzed using SPSS ver. 18 IBM® incorporation.
- Numerical data were tested for normality with D'agostino-pearson test, normally distributed data were presented as mean ± SD, and non-normally distributed data were presented as median (interquartile range).
- Categorical data were presented as number and percent of total.
- Comparative analysis of numerical data was done with unpaired student t test, or Mann-Whitney test deepening on normality of data.

- Comparative analysis of categorical data was done with Chi-square (X2), and Fisher exact test.
- Comparison of paired data was done with Paired sample t test, or Wilcoxon signed rank test, for parametric and non-parametric data respectively.
- Data were tabulated and graphically illustrated.

RESULTS

One Hundred patients were included in the study that was conducted in Ain Shams university hospitals between September 2014 and February 2016. Patients were divided into 2 groups: Group A (received preoperative dose of Dexamethasone) and group B (did not receive Dexamethasone). Patients' data are shown in the following tables.

Table (1): Demographics and clinical data.

		Dexamethasone				**P Value**
		Yes		**No**		
		Mean	**SD**	**Mean**	**SD**	
Age (Years)		36.7	8.5	36.4	9.1	0.987
Gender	**Male**	0		7 (13.2%)		0. 154
	Female	47 (100%)		46 86.8%)		

100 patients in the study (47 in group A and 53 in group B) presented with benign thyroid disease for which total thyroidectomy was done. There was no statistically significant difference between the two groups as regards age and sex.

Baseline voice recording (preoperative voice recordings):

Table (2): Descriptive analysis for patients' preoperative voice recordings as regard Dysphonia, Strained voice, Leaky voices and voice irregularity.

		Frequency	**Percent**
Dysphonia	**Normal**	63	63
	Mild	30	30
	Moderate	7	7
Strained	**Normal**	90	90
	Mild	7	7
	Moderate	3	3
Leaky	**Normal**	80	80
	Mild	13	13
	Moderate	3	3
	Severe	4	4
Irregular	**Normal**	93	93
	Mild	4	4
	Moderate	3	3

Table (3): Comparison between both groups as regard baseline voice recording data.

		Dexamethasone therapy				P Value
		No (53)		Yes (47)		
		number	%	number	%	
Grade of Dysphonia	Normal	36	68.75%	27	57%	0.265
	Mild	10	18.75%	20	43%	
	Moderate	7	12.50%	0	0%	
Strained	Normal	50	94%	40	86%	0.209
	Mild	0	0%	7	14%	
	Moderate	3	6%	0	0%	
Leaky	Normal	43	81%	37	79%	0.453
	Mild	4	7%	10	21%	
	Moderate	3	6%	0	0%	
	Severe	3	6%	0	0%	
Irregular	Normal	50	94%	44	93%	0.724
	Mild	0	0%	3	7%	
	Moderate	3	6%	0	0%	

As shown in the table there is no statistical difference between the two study groups as regards baseline voice recording data.

Table (4): Comparison of voice recording parameters before and after operation in group (A)

Dexamethasone group(A) (47)						
		Before		After		P Value
		Count	%	Count	%	
Grade of Dysphonia	Normal	27	57.1%	44	92.9%	**0.025**
	Mild	20	42.9%	3	7.1%	
	Moderate	0	0.0%	0	0.0%	
	Severe	0	0.0%	0	0.0%	
Strained	Normal	40	85.7%	47	100.0%	0.16
	Mild	7	14.3%	0	0.0%	
	Moderate	0	0.0%	0	0.0%	
	Severe	0	0.0%	0	0.0%	
Leaky	Normal	37	78.6%	44	92.9%	0.16
	Mild	10	21.4%	3	7.1%	
	Moderate	0	0.0%	0	0.0%	
	Severe	0	0.0%	0	0.0%	
Irregular	Normal	44	92.9%	44	92.9%	1
	Mild	3	7.1%	3	7.1%	
	Moderate	0	0.0%	0	0.0%	
	Severe	0	0.0%	0	0.0%	

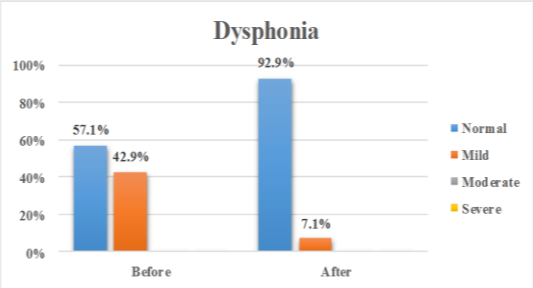

Fig. (2): pre and post-operative dysphonia in dexamethasone group

There are significant changes in results of dysphonia with P value 0.025 in dexamethasone group, other voice recording parameters showed no significant changes compared to preoperative levels.

- **Baseline (pre-operative) Aerodynamics:**

Table (5): a comparison between the 2 study groups as regard baseline aerodynamic parameters; F0, Jitter, and Shimmer.

	Dexamethasone				P Value
	Yes		No		
	Mean	SD	Mean	SD	
Fundamental frequency	225.6	37.5	208.8	38	0.242
Jitter	1.88	0.99	1.66	1.2	0.59
Shimmer (dB)	4.2	2.35	3.43	1.5	0.28

The previous table shows no significant differences between two groups as regard the pre-operative baseline aerodynamic parameters**.**

- **Postoperative Aerodynamics:**

Table (6) comparison between the two groups in postoperative aerodynamics

	Dexamethasone				P Value
	Yes		No		
	Mean	SD	Mean	SD	
Fundamental frequency	172.44	54.51	180.79	53.6	0.443
Jitter	2.5	1.41	2.2	1.8	0.363
Shimmer (dB)	5.86	3.2	3.56	1.64	**0.017**

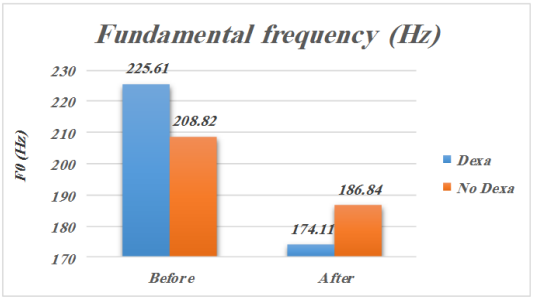

Fig. (3) chart comparing changes of F0 results before and after operation in each group

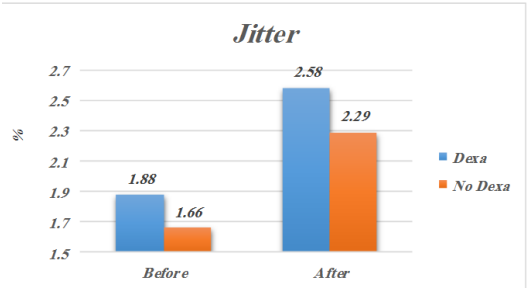

Fig. (4): chart showing values of Jitter test before and after the operation in both groups

Fig. (5): chart showing values of Shimmer before and after the operation in both groups**.**

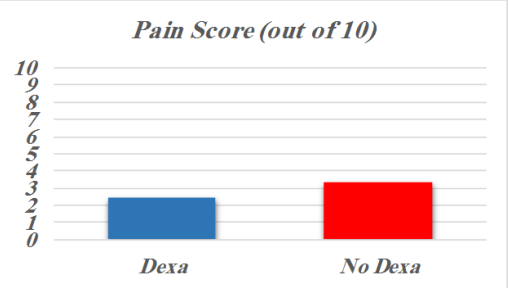

Fig.e (6): Comparison between two groups in postoperative Pain Score.

Postoperative analysis of aerodynamics show close results as regard fundamental frequency and Jitter however the Shimmer values showed significantly different values between the two groups.

- **Post-operative Dyspepsia:**

The following table illustrates comparison between the two groups as regard postoperative Nausea and vomiting (Dyspepsia).

Table (7): comparison between the two groups as regard postoperative Dyspepsia.

	Dexa (47)		No Dexa (53)		P
	Count	**%**	**Count**	**%**	**Value**
Nausea and Vomiting	0	0	7	12.5%	0.485

The study showed that 12.5 % of patients who didn't receive Dexamethasone experienced various degrees of dyspepsia while no patients from group A suffered from dyspepsia. However, the study showed no statistically significant differences between the two groups.

- **Post-operative pain:**

The two groups were compared as regard postoperative pain.

Table (7): Comparison between two groups in postoperative Pain Score

	Dexa (47)		No Dexa (53)		P
	Mean	**SD**	**Mean**	**SD**	**Value**
Pain	2.43	0.64	3.31	0.95	**0.006**

The study of postoperative pain showed a highly significant difference between the dexamethasone group and the control group, where Group A patients showed lower values of average pain score (2.43) compared to Group B patients who didn't receive Dexamethasone (3.31).

DISCUSSION

Thyroidectomy is one of the most common elective surgical procedures in the western world [(1)]. After thyroidectomy the incidence of postoperative nausea and vomiting (PONV) is 70-80% when no prophylactic antiemetic therapy is given [(3)]. The exact mechanism of thyroidectomy-related nausea and vomiting is assumed to be attributed to significant edema and inflammation of the neck tissues which may persistently evoke parasympathetic impulses through the Vagus, recurrent laryngeal and glossopharyngeal nerves to the vomiting center, thus initiating vomiting responses [(8)].

Vocal dysfunction is another important and feared complication of thyroid surgery. Operative injury to the recurrent laryngeal nerve is often considered to be the main cause of voice alterations, and its prevalence varies from 0.77% to 13.3%. However, alterations in vocal quality can also be found in the absence of injuries of the laryngeal nerve. Multiple causes of these postoperative voice alterations have been described by several authors, such as for instance operative injury as arytenoid injury or dysfunction of the pre-thyroid strap muscles influencing pitch control. Other possible causes of postoperative voice alterations are slight modifications of the vascular supply and/or venous drainage of the larynx resulting in mucosal changes. Oro-tracheal

intubation may also have an effect. The psychological reaction and a loss of general fitness after the surgery can also lead to a weaker voice [(7)].

Computer programs that allow voice recording permit investigators to avoid subjective factors in the evaluation of voice alterations by the patient and the observer [(9)].

In this study the effect of use of prophylactic dose of Dexamethasone on postoperative nausea, vomiting, pain and voice dysfunction have been discussed.

We conducted our study in the endocrine surgery unit; general surgery department at Ain Shams University hospitals between September 2014 and February 2016 to study the effect of preoperative dose of Dexamethasone on postoperative Nausea, vomiting and voice changes on 100 patients undergoing total thyroidectomy without recurrent laryngeal nerve injury. All cases of our study underwent total thyroidectomy for benign thyroid disorders. Malignant disorders were excluded to exclude malignant infiltration of laryngeal nerve or vocal folds as a possible cause of voice change.

In our study the mean age was 36.5 years, Females represented 93%, while 13% were males. The study included 100 patients. Group (A) included 47 patients and group (B) included 53 patients. Both groups were compared as regard pre-operative (baseline) and post-operative voice recording and also pre-operative and post-operative aerodynamic assessment (Fundamental frequency, Jitter, Shimmer (dB). Other parameters included post-operative dyspepsia and post-operative pain.

Our study showed that there was no difference between both groups as regards any of the pre-operative parameters.

Concerning **Postoperative voice recording parameters;** our study showed a significant difference between both groups as regards dysphonia. This demonstrates the significant role of Dexamethasone in lowering the incidence of postoperative dysphonia. In agreement with our study, **Feroci et al.** [(10)] reported a significant difference between the two groups where the dexamethasone group showed significantly lower incidence rate of postoperative dysphonia and strained voice compared to the group who did not receive dexamethasone. This can be attributed to the anti-inflammatory effect of steroids to decrease oedema and limit tissue inflammatory response.

In disagreement to our study **Worni et al.**[(11)] showed that no significant difference could be noticed as regards dysphonia and voice strain. Perhaps this is attributed to the inclusion of malignant thyroid diseases in their study inclusion criteria.

Regarding **Postoperative Aerodynamics** Our study concluded that Postoperative analysis of aerodynamics showed no significant difference between the study groups as regards fundamental frequency and Jitter. However, the Shimmer values showed significant difference between the two groups. In agreement with our study **Feroci et al., 2011**[(10)] reported significant differences in terms of Jitter and Shimmer parameters, while fundamental frequency showed no statistically different results. **Worni et al., 2008**[(11)] study showed no significant difference as regards aerodynamic parameters. Again, this might have resulted from smaller study population and different inclusion criteria.

As regards **Post-operative pain** Our study showed that Group A (dexamethasone group) demonstrated significantly lower postoperative average pain score (2.43) compared to the other group (3.31). In agreement with our study both **Worni et al.**[(11)] and **Feroci et al.**[(10)] studies showed highly significant difference between the dexamethasone group and the other group, this is well explained by the anti-inflammatory effect of the corticosteroids which help to minimize the body response to inflammation by inhibiting the release of inflammatory mediators and pain producing substances.

As regards **Post-operative Dyspepsia** The study showed that 12.5 % of patients who didn't receive Dexamethasone experienced various degrees of dyspepsia while no patients from group A suffered from dyspepsia. However the study showed no statistically significant differences between the two groups. **Feroci et al.**[(10)] study however did not show any statistically significant values among their two study groups. Despite the proven effect of corticosteroids as a potent anti-emetic and their popular use in cancer patients to minimize chemotherapy effects, this can be more significant in studies on GIT operations which are usually accompanied by GIT upset symptoms or can be well noticed in larger scale studies.

In contrast to our study **Worni et al.**[11] showed significant statistical values as regard postoperative nausea and vomiting, and this also may be attributed to the inclusion of malignant thyroid diseases that were diagnosed preoperatively and some had already received chemotherapeutic agents.

CONCLUSION

A preoperative single dose of dexamethasone can effectively reduce nausea, vomiting, and pain, and improve postoperative voice function so that this strategy can be routinely applied in thyroidectomy operations.

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